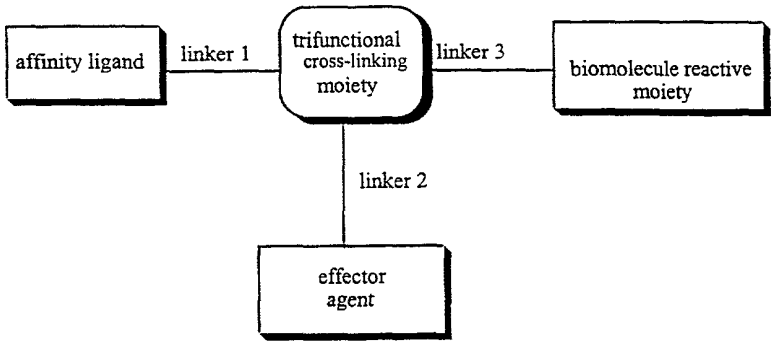
CLAIMS

1. Reagent for conjugation to a biomolecule, wherein the reagent is a single molecule with at least three functional parts and has the following schematic structure (I):



a) wherein a trifunctional cross-linking moiety is coupled to

b) an affinity ligand via a linker 1, said affinity ligand being capable of binding with another molecule having affinity for said ligand, to

c) an effector agent, optionally via a linker 2, said effector agent exerting its effect on cells, tissues and/or humorous molecules in vivo or ex vivo, and to

d) a biomolecule reactive moiety, optionally via a linker 3, said moiety being capable of forming a bond between the reagent and the biomolecule.

2. Reagent according to claim 1, wherein the trifunctional cross-linking moiety is chosen from the group consisting of triaminobenzene, tricarboxybenzene, dicarboxyaniline and diaminobenzoic acid.

3. Reagent according to claims 1 and 2, wherein the affinity ligand is a moiety that binds with another molecule with an affinity constant of 10^6 M^{-1} or higher.

4. Reagent according to claims 1-3, wherein the affinity ligand is a moiety which binds specifically to avidin, streptavidin or any other derivatives, mutants or fragments of avidin or streptavidin having essentially the same binding function to the affinity ligand.

5. Reagent according to claims 1-4, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin.

6. Reagent according to claims 1-5, wherein the biotin derivative is chosen from the group consisting of norbiotin, homobiotin, oxybiotin, iminobiotin, desthiobiotin, diaminobiotin, biotin sulfoxide, and biotin sulfone, or other molecules thereof that having essentially the same binding function.

7. Reagent according to claim 5, wherein the stability towards enzymatic cleavage, preferably by bioinidase, of the biotinamide bond to release biotin has been improved by using biotin derivatives, preferably norbiotin or homobiotin.

8. Reagent according to claims 1-6, wherein linker 1 serves as an attaching moiety and a spacer between the trifunctional cross-linking moiety and the biotin moiety such that binding with avidin or streptavidin, or any other biotin binding species, is not diminished by steric hindrance.

9. Reagent according to claims 1-8, wherein linker 1 contains hydrogen bonding atoms such as ethers or thioethers, or ionizable groups such as carboxylates, sulfon-

ates, or ammonium groups to aid in water solubilization of the biotin moiety.

10. Reagent according to claims 1-9, wherein stability towards enzymatic cleavage, preferably by biotinidase, of the biotinamide bond to release biotin have been improved by introducing an alpha carboxylate or an N-methyl group in linker 1.

11. Reagent according to claim 1, wherein the effector agent is chosen from the group consisting of synthetic or natural occurring toxins, enzymes, preferably enzymes capable of converting a pro-drug to an active drug, hormones, immunosuppressive agents, immunostimulating agents, radionuclide binding/bonding moieties, radiosensitizers, enhancers for X-ray or MRI or ultrasound, non-radioactive elements which can be converted to radioactive elements by means of external irradiation after that the biomolecule carrying said element has been accumulated to specific cells or tissues, or compounds used in photoimaging or photodynamic therapy.

12. Reagent according to claims 1-11, wherein the effector agent is a radionuclide binding/bonding moiety to which radionuclides can be bound by chelation or covalent bonding.

13. Reagent according to claim 7, wherein the effector agent is a radionuclide binding/bonding moiety to which radionuclides are bound by chelation or through covalent bonding.

14. Reagent according to claims 1-13, wherein the effector agent comprises aryl halides and vinyl halides for radionuclides of halogens, amino-carboxy derivatives, preferably EDTA and DTPA derivatives, including Me-DTPA, CITC-DTPA, and cyclohexyl-DTPA, and cyclic amines, pre-

ferably NOTA, DOTA, and TETA for In, Y, Pb, Bi, Cu, Sm, and Lu radionuclides.

15. Reagent according to claims 1-14, wherein the effector agent is provided with positron imaging radionuclides, preferably F-18, Br-75, Br-76, and I-124; therapeutic radionuclides, preferably Y-90, I-131, In-114m, Re-186, Re-188, Cu-67, Sm-157, Lu-177, Bi-212, Bi-213, At-211, Ra-223; and gamma imaging radionuclides, preferably Tc-99m, In-111 and I-123.

16. Reagent according to claims 1-11, wherein the effector agent is a photoactive compound or a compound which can be converted to a photoactive compound, preferably a chromophore or fluorophore or alike compound.

17. Reagent according to claims 1-16, wherein linker 2 is excluded.

18. Reagent according to claims 1-16, wherein linker 2 provides a spacer length of 1-25 atoms, preferably a length of 6-18 atoms, or groups of atoms.

19. Reagent according to claims 1-16, and 18, wherein linker 2 contains hydrogen bonding atoms, preferably ethers or thioethers, or ionizable groups, preferably carboxylates, sulfonates, or ammonium groups, to aid in water solubilization.

20. Reagent according to claims 1-19, wherein the biomolecule reactive moiety is chosen from the group consisting of active esters, preferably N-hydroxy-succinimide esters, sulfo-N-hydroxysuccinimide esters, phenolic esters, aryl and alkyl imitates, alkyl or aryl isocyanates or isothiocyanates reacting with amino groups on the biomolecule, or maleimides or alpha-haloamides reacting with sulfhydryl groups on the biomolecule, or aryl or alkylhydrazines or alkyl or aryl hydroxylamines

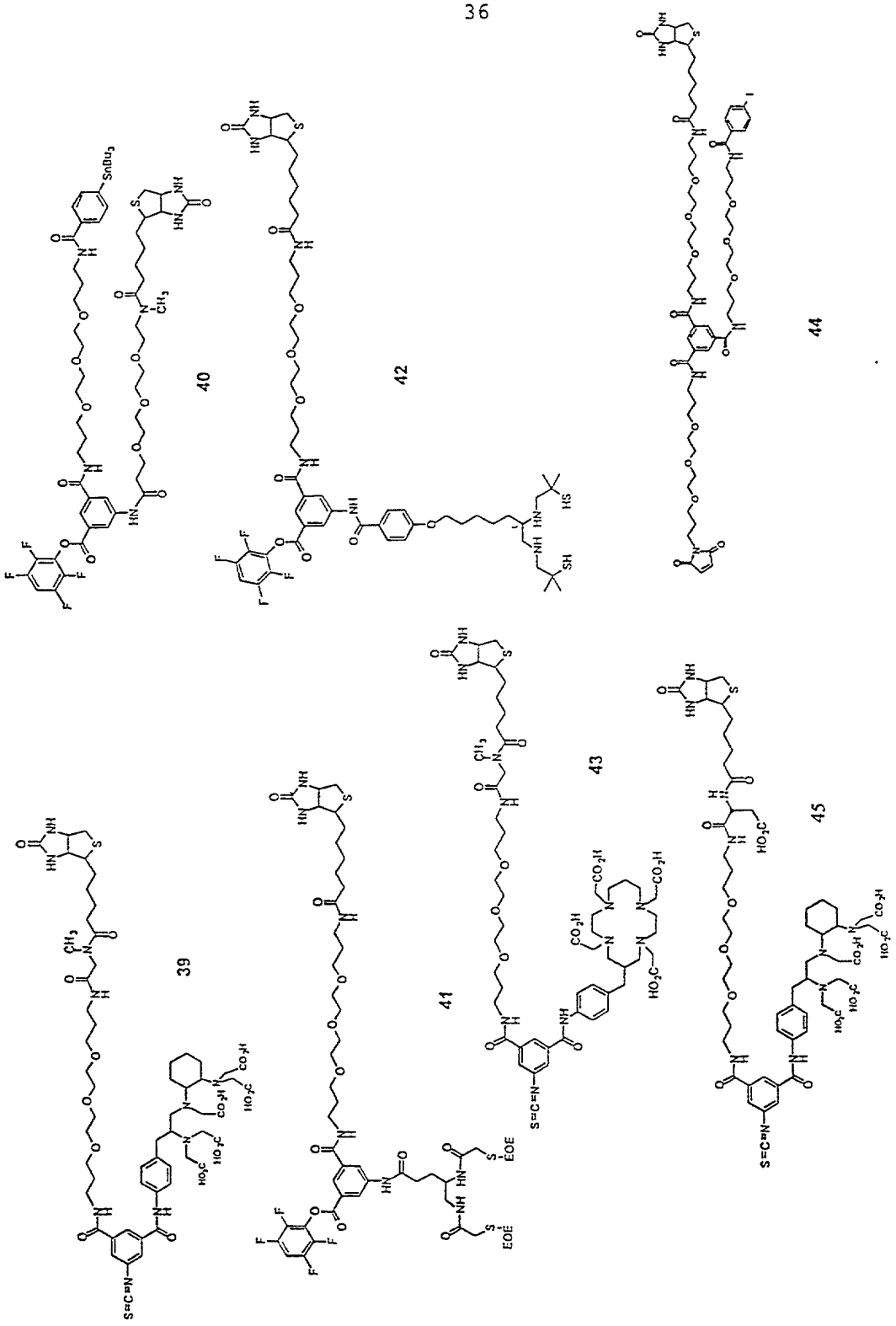
reacting with aldehyde or ketone groups naturally occurring or synthetically produced on the biomolecule.

21. Reagent according to claims 1-20, wherein linker 3 is excluded.

22. Reagent according to claims 1-20, wherein linker 3 provides a spacer of a length of 1-25 atoms, preferably a length of 6-18 atoms, or groups of atoms.

23. Reagent according to claims 1-20 and 22, wherein linker 3 contains hydrogen bonding atoms such as ethers or thioethers, or ionizable groups, preferably as carboxylates, sulfonates, or ammonium groups to aid in water solubilization.

24. Reagent according to any of the previous claims, wherein it is chosen from the group consisting of the following compounds:



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25. Reagent according to claim 1, wherein more than one affinity ligand and/or more than one effector agent are bound to a trifunctional or tetrafunctional cross-linking group.

26. Reagent according to any of the previous claims for diagnosis and treatment of human and animal conditions or diseases, preferably in targeting of cancer, myocardial infarcts, deep vein thrombosis, stroke loci, pulmonary embolism and atherosclerosis.

27. Reagent according to any of claims 1-25 for the in vitro analysis of affinity labelled biomolecules, preferably biomolecules labelled with biotin or derivatives thereof, wherein the amount of affinity label bound to the biomolecule is determined.

28. Method for diagnosis or treatment of a mammalian condition or disease, wherein a reagent according to any of the previous claims is conjugated to a biomolecule, and wherein said conjugated biomolecule is added to the blood circulation of a mammal and kept therein for a certain time in order to be concentrated to the target tissue or cells on which it is to be detected and/or exert its therapeutic action, wherein the conjugated biomolecules not being attached to the target tissue is completely or partially removed from blood circulation by the administration of a protein specifically binding to the affinity ligand or by passing the mammalian blood or plasma through an affinity column specifically adsorbing the conjugated biomolecule by specific interaction with the affinity ligand.

29. Method for diagnosis or treatment of a mammalian condition or disease, wherein a reagent according to any of claims 1-26 provided with a radionuclide is conjugated to a biomolecule, or alternatively, the reagent is

conjugated to the biomolecule prior to attachment of the radionuclide, and the said radioactive conjugated biomolecule is added to the blood circulation of a mammal and kept therein for a certain period of time in order to be concentrated to the target tissue or cells on which it is to be detected and/or exert its therapeutic action, wherein the biomolecules that are not being attached to the target tissue are completely or partially removed from the blood circulation by administration of a protein specifically binding to the affinity ligand or by passing the mammalian blood or plasma through an affinity column specifically adsorbing the conjugated biomolecule by specific interaction with the affinity ligand.

30. Kit for extracorporeally eliminating or at least reducing the concentration of a non-tissue-bound therapeutic or diagnostic biomolecule conjugate, which has been introduced to a mammalian host and kept therein for a certain time in order to be concentrated to the specific tissues or cells by being attached thereto, in the plasma or whole blood of the vertebrate host, said kit comprising a therapeutic or diagnostic biomolecule, a reagent according to any of claims 1-26 for simultaneous conjugation of an affinity ligand and an effector agent to a biomolecule, means for extracorporeal circulation of whole blood or plasma from the vertebrate host, an optional plasma separation device for separation of plasma from blood, an extracorporeal adsorption device, and a means for return of whole blood or plasma without or with low concentration of non-tissue-bound target specific therapeutic or diagnostic agent to the mammalian host, wherein the adsorption device comprises immobilized receptors specific towards an affinity ligand.

31. A kit according to claim 30, wherein the effector agent is chosen from the group consisting of synthetic or naturally occurring toxins, enzymes capable of converting a pro-drug to an active drug, immunosuppressive agents, immunostimulating agents, and radionuclide binding/bonding moieties with or without the radionuclide.

32. A kit according to claims 30 and 31, wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, and the immobilized receptor is avidin or streptavidin, or any other derivatives, mutants or fragments of streptavidin having essentially the same binding function to biotin.